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Authors

Krishnan, Usha
Mousa, Hayat
Dall'Oglio, Luigi
et al.

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ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Esophageal Atresia-Tracheoesophageal Fistula

*†Usha Krishnan, ‡§Hayat Mousa, ||Luigi Dall'Oglio, †¶Nusrat Homaira, #**Rachel Rosen, ††‡‡Christophe Faure, and §§Frédéric Gottrand

ABSTRACT

Background: Esophageal atresia (EA) is one of the most common congenital digestive anomalies. With improvements in surgical techniques and intensive care treatments, the focus of care of these patients has shifted from mortality to morbidity and quality-of-life issues. These children face gastrointestinal (GI) problems not only in early childhood but also through adolescence and adulthood. There is, however, currently a lack of a systematic approach to the care of these patients. The GI working group of International Network on Esophageal Atresia comprises members from ESPGHAN/NASPGHAN and was charged with the task of developing uniform evidence-based guidelines for the management of GI complications in children with EA.

Methods: Thirty-six clinical questions addressing the diagnosis, treatment, and prognosis of the common GI complications in patients with EA were formulated. Questions on the diagnosis, and treatment of gastroesophageal reflux, management of ''cyanotic spells,'' etiology, investigation and management of dysphagia, feeding difficulties, anastomotic strictures, congenital esophageal stenosis in EA patients were addressed. The importance of excluding eosinophilic esophagitis and associated GI anomalies in symptomatic patients with EA is discussed as is the quality of life of these patients and the importance of a systematic transition of care to adulthood. A systematic literature search was performed from inception to March 2014 using Embase, MEDLINE, the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Clinical Trials, and PsychInfo databases. The approach of the Grading of Recommendations Assessment, Development and Evaluation was applied to evaluate outcomes. During 2 consensus meetings, all recommendations were discussed and finalized. The group members voted on each recommendation, using the nominal voting technique. Expert opinion was used where no randomized controlled trials were available to support the recommendation.

Key Words: anastomotic stricture, dysphagia, esophageal atresia, esophageal carcinoma, guidelines, transition

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Esophageal atresia (EA) is one of the most common digestive malformation occurring in 1 in 2,400 to 4,500 births worldwide (1). Since the first successful primary repair by Cameron Haight in 1941, postoperative outcomes have changed. With the exception of patients experiencing severe concomitant malformations such as congenital heart disease, improvements in operative, and perioperative care issues have shifted the focus from mortality to morbidity and quality-of-life issues (2–4). EA is no more just a neonatal surgical problem but a lifelong problem.

Other than respiratory problems, nutritional and gastrointestinal (GI) issues are prevalent not only in the first years of life but also in adolescence and adulthood. Gastroesophageal reflux (GER), peptic esophagitis, gastric metaplasia and Barrett esophagus, anastomotic strictures (AS), feeding disorders, dysphagia, esophageal dysmotility are the most frequent GI short- and long-term complications encountered in children and adolescents. Concerns in adults include esophageal adenocarcinoma and epidermoid carcinoma, which have been recently been reported (3).

To date, although morbidity is well known and the need for careful multidisciplinary follow-up is highlighted, no recommendations on the GI and nutritional management of infants and children with EA are available. There is currently a lack of a systematic approach for the care of these patients not only during childhood but through transition to adulthood. Hence, the International Network on Esophageal Atresia (INoEA) was formed in 2013 to help formulate clinical practice guidelines for the care of these patients.

METHODS

The project started in February 2014, when under the auspices of INoEA, a working group consisting of selected members including both pediatric gastroenterologists and a pediatric surgeon

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From the *Department of Pediatric Gastroenterology, Sydney Children's Hospital, the †Discipline of Pediatrics, School of Women's and Children's Health, University of New South Wales, Sydney, Australia, the ‡Division of Pediatric Gastroenterology, Rady Children's Hospital, the §San Diego School of Medicine, University of California, San Diego, the ||Digestive Endoscopy and Surgery Unit, Bambino Gesu Children's Hospital-IRCCS, Rome, Italy, the ¶Centre for Big Data Research in Health, University of New South Wales, Sydney, Australia, the #Aerodigestive Centre, Division of Gastroenterology and Nutrition, Boston Children's Hospital, Boston, the **Harvard Medical School, Harvard, MA, the ††Division of Pediatric Gastroenterology, Sainte-Justine Hospital, the ‡‡Department of Pediatrics, Université de Montréal, Montreal, Canada, and the §§CHU Lille, University Lille, National Reference Center for Congenital Malformation of the Esophagus, Department of Pediatric Gastroenterology Hepatology and Nutrition, Lille, France.

Address correspondence and reprint requests to Christophe Faure, MD, Division of Pediatric Gastroenterology, Sainte-Justine Hospital 3715 Côte Sainte Catherine, H3T1C5 Montreal, Quebec, Canada (e-mail: christophe.faure@umontreal.ca).

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from ESPGHAN and NASPGHAN was formed to look at formulating evidence-based clinical practice guidelines based on current knowledge for the evaluation and treatment of GI and nutritional complications in children with EA. Clinical questions relevant for the evaluation and treatment of GI and nutritional complications in children with EA and tracheoesophageal fistula (TEF) were formulated (Table 1).

The questions were formulated by the members of the working group on GI morbidity in children with EA. Members of this working group included both ESPGHAN/NASPGHAN members. After the questions were formulated, the guidelines committee was subdivided into subgroups based on expertise of the individual members and dealt with the questions under each of the sections separately. Questions were answered using the results of systematic literature searches and based on expert opinion.

Systematic literature searches were performed by a clinical librarian with help from one of the authors (U.K.) from inception to March 2014. The EMBASE, MEDLINE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Clinical Trials, and PsychInfo databases were searched. Inclusion criteria were as follows:

(1) Systematic reviews, prospective or retrospective controlled studies, prospective or retrospective cohort studies.
(2) Study population consisting of children 0 to 18 years of age and adults with EA.
(3) The key words used to identify relevant papers were EA, TEF, congenital esophageal stenosis (CES).

Additional strategies for identifying studies included using the key words mentioned above to search in the reference lists of review articles and the included studies. Furthermore, all of the members of the guidelines committee were asked to search the literature relevant to their assigned topics to possibly uncover further studies that may have been missed by the former search. After the creation of the initial reference list of review articles and studies, articles published before 1980, articles in languages other than English and French, animal studies and case reports with fewer than 5 patients, and abstracts presented only during conference proceedings were excluded.

The approach of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) was used to identify outcomes (5–10). The levels and quality of evidence were assessed using the classification system of the Oxford Centre for Evidence-Based Medicine (*http://www.cebm.net*) (diagnostic and prognostic questions) and the GRADE system (therapeutic questions). Grades of evidence for each statement are based on the grading of the literature. If no therapeutic studies were found, we decided to define the quality of evidence as ''low.'' Using the GRADE system, the quality of evidence was graded as follows (5–10):

(1) **High:** Further research is unlikely to change our confidence in the estimate of effect.
(2) **Moderate**: Further research is likely to have impact on our confidence in the estimate of effect and may change the estimate.
(3) **Low:** Further research is likely to have an impact on our confidence in the estimate of effect and likely to change the estimate.
(4) **Very low**: Any estimate of effect is uncertain.

One of the authors (U.K.) systematically reviewed all the articles selected in the literature review and summarized the important findings in a tabular form. Subsequently a qualified

TABLE 1. Overview of clinical questions

1. GER in EA patients
   a. Should GER be systematically treated in all EA patients in the neonatal period?
   b. How should GER be managed?
   c. How long should GER be treated?
2. Role of reflux testing in EA patients
   a. What is the role of 24-hour pH and pH-impedance monitoring in EA patients?
   b. What is the role of esophagoscopy in EA patients?
   c. How should GER be monitored, and when?
   d. How often do EA patients need surveillance endoscopy in childhood and adolescence?
3. Fundoplication
   a. What is the role of fundoplication in EA patients with GER?
   b. What evaluations should be performed before fundoplication?
4. Extraesophageal manifestations of GER and dysmotility
   a. What extra esophageal manifestations of reflux and dysmotility are seen in EA patients?
   b. How should clinicians investigate extraesophageal manifestations in EA patients?
   c. How should clinicians treat extraesophageal manifestations in EA patients?
5. How to investigate and manage ''Dying/cyanotic spells'' in EA patients?
6. Dysphagia and esophageal function
   a. When should dysphagia be considered in patients with in EA?
   b. How to investigate dysphagia in EA patients?
   c. What is the role of esophageal manometry in EA patients with dysphagia?
   d. How should dysphagia be managed in EA patients?
   e. How should dysphagia in EA patients postfundoplication be investigated?
   f. How should dysphagia in EA patients postfundoplication be managed?
7. When should we look for associated vascular abnormalities in EA?
8. Feeding and nutrition
   a. How should abnormal feeding behaviors in EA be prevented and managed?
   b. Is there a risk for malnutrition in infants, children and adolescents with EA?
9. Anastomotic stricture
   a. What is the definition of a clinically relevant anastomotic stricture in patients with EA?
   b. When should anastomotic strictures in EA be diagnosed?
   c. How should anastomotic stricture be diagnosed in EA?
   d. How anastomotic strictures be managed?
   e. What is the definition of recurrent anastomotic stricture in EA patients?
   f. What adjuvant treatments are available in recurrent strictures in EA patients?
10. How to diagnose and manage congenital stricture in EA?
11. Eosinophilic esophagitis and other GI anomalies
   a. What is the impact of eosinophilic esophagitis on symptoms in EA patients?
   b. How should eosinophilic esophagitis be diagnosed and managed in EA patients?
12. What are the other GI conditions (apart from anal stenosis/anorectal malformations) that can be associated with EA?
13. Transition to adulthood and quality of life
   a. What are the long-term digestive morbidities of EA in adulthood?
   b. Is medical transitioning to adult medicosurgical services necessary?
   c. How should surveillance be managed in adult EA patients after transition from childhood?
   d. Is QOL impaired in EA patients?

EA = esophageal atresia; GER = gastroesophageal reflux; GI = gastrointestinal.

epidemiologist (N.H.) systematically reviewed and graded, using the GRADE system, the papers chosen in the literature review. Both the summary tables of all the articles and their grading (Supplemental Digital Content 1, Summary Tables, *http://links.lww.com/MPG/A776*) were sent to all the authors before they wrote their relevant sections. (Online-only appendix [Supplemental Digital Content 2, Appendix, *http://links.lww.com/MPG/A777*] lists the quality assessment of all included studies.)

Consensus Meeting and Voting

Two consensus meetings were held to achieve consensus on and formulate all of the recommendations: October 2014 and February 2015. Each subgroup presented the recommendations during the consensus meetings, wherein these were then discussed and modified according to the comments of the attendees. The consensus was formally achieved through nominal group technique, a structured quantitative method. The group consisting of members of all the subgroups (U.K., H.M., L.D., R.R., C.F., and F.G.) anonymously voted on each recommendation. A 9-point scale was used (1—strongly disagree to 9—fully agree), and votes are reported for each recommendation. It was decided in advance that consensus was reached, if >75% of the working group members voted 6, 7, 8, or 9. The consensus was reached for all of the questions. A decision was made to present 3 algorithms (Figs. 1–3). The final draft of the guidelines was sent to all of the committee members for approval in October 2015, and then critically reviewed by a multidisciplinary panel of members of the INoEA (see Acknowledgement).

• Gastroesophageal reflux (GER)

1. Should GER be systematically treated in all EA patients in the neonatal period? (Fig. 1, box 1)

No study has been published that reports the prevalence of GER in neonates following surgery for EA. In EA patients, GER is, however, the most frequent GI tract complication with a reported prevalence of 22% to 45% (Table 2), especially in infants and children with isolated EA in whom GER is reported in almost all patients (11).

GER is associated with complications in neonates and infants undergoing surgery for EA. Uncontrolled studies suggest that GER is a major factor for recurrent AS (12–14).

Pulmonary complications associated with GER are persistent atelectasis, aspiration pneumonia, asthma/increased airway reactivity, chronic lung disease with bronchectasis, and worsened tracheomalacia (12,14). Airway obstruction and/or acute life-threatening episodes (ALTE) can result from either proximal GER reaching the larynx or GER in lower esophagus that could be reflexively responsible for respiratory symptoms (15). (During the editorial processing, the term Brief Resolved Unexplained Event (BRUE) has been proposed to replace the term ALTE by the American Academy of Pediatrics [Tieder JS, et al. Brief resolved unexplained events (formerly apparent life-threatening events) and evaluation of lower-risk infants. *Pediatrics* 2016;137 (5).] A BRUE is defined as an event occurring in an infant younger than 1 year when the observer reports a sudden, brief, and now resolved episode of ≥1 of the following: cyanosis or pallor; absent, decreased, or irregular breathing; marked change in tone (hyper- or hypotonia); and altered level of responsiveness. A BRUE is diagnosed only when there is no explanation for a qualifying event after conducting an appropriate history and physical examination. By using this definition and framework, children with EA-TEF, either < or >1 year of age, who present with a BRUE must be considered at high risk and must not be considered as ''unexplained.'' They should be managed according to the present recommendations.)

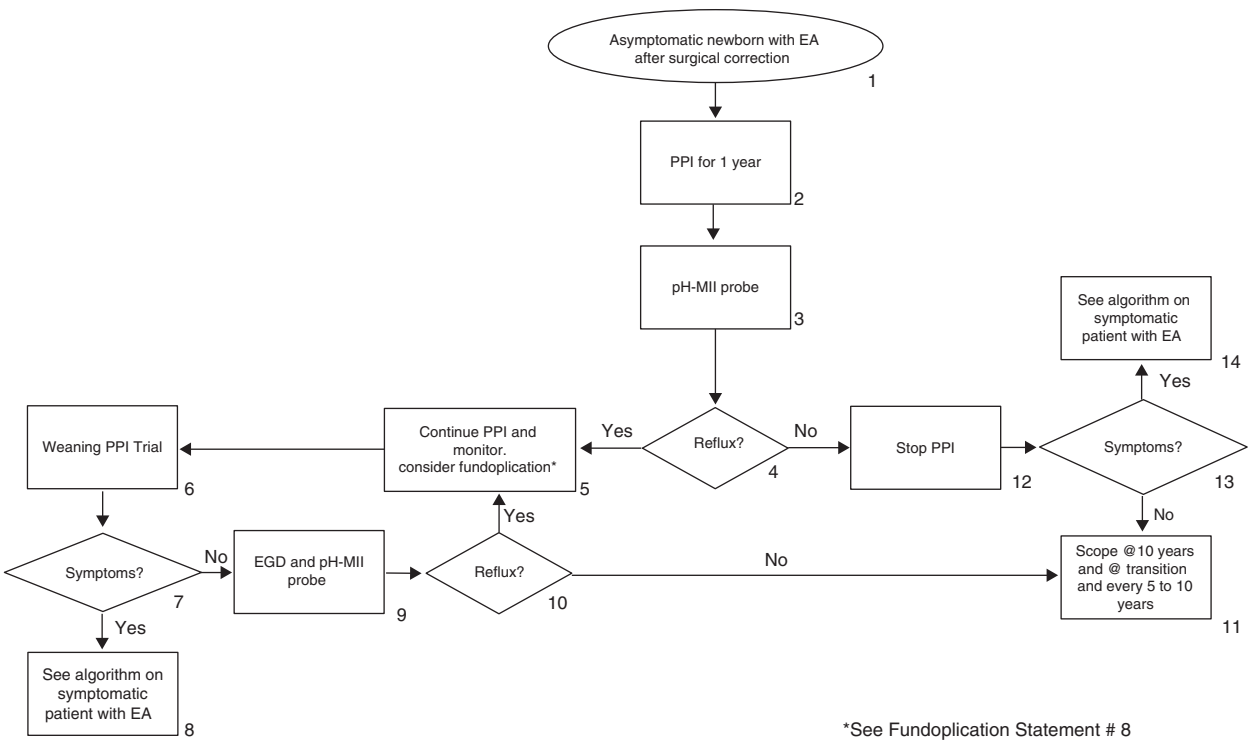

FIGURE 1. Algorithm for the evaluation and treatment of an asymptomatic newborn after surgical correction of an esophageal atresia. EA = esophageal atresia; EGD = esogastroduodenoscopy; pH-MII = pH-impedance; PPI = proton pump inhibitor.

TABLE 2. Prevalence of gastroesophageal reflux, esophagitis, and fundoplication in patients with esophageal atresia

References	Number	Age at evaluation	Prevalence of GER	Diagnosis of GER	Prevalence of esophagitis	Prevalence of antireflux surgery
Curci and Dibbins (86)	36	NA	NA	NA	NA	45%
Montgomery and Frenckner (69)	110	NA	30%	Barium study	NA	8%
Engum et al (172)	227	1 mo–22 y (mean: 6)	58%	NA	NA	44%
Chetcuti et al (46)	125	>18 y	46% (11% >1 episode a week)	Clinical signs (heartburn)	NA	NA
Somppi et al (173)	42	3–30 y (mean: 12.6)	22%	pH-metry	6% 51% (histo)	8%
Krug et al (32)	39	18–26 y	33%	Clinical score	23%	NA
Bergmeijer et al (35)	125	NA	NA	NA	NA	23%
Yanchar et al (174)	90 excluding type A	NA	46%	NA	NA	33%
Deurloo et al (14)	371	1–54 y	40%	pH-metry	NA	23%
Deurloo et al (31)	40	28–45 y (mean: 34)	52%	Heartburn retrosternal pain	9% (90% histo)	2.5%
Koivusalo et al (175)	50	2.5–95 mo (mean: 9.2)	20%	pH-metry	26%	24%
Konkin et al (176)	144	Postoperative period	31%	NA	NA	12%
Taylor et al (159)	132	20–48 y (mean: 33)	63%	Symptoms	58% (histo)	11%
Koivusalo et al (30)	61 type C	1–10 y (median 5 y)	46%	Fundoplication or pH-metry or endoscopy	NA	30%
Castilloux et al (4)	134	0.3–16 y (mean: 5)	<1 y, 34% >1 y, 43%	Severe GER: moderate to severe esophagitis on biopsy and/or intestinal metaplasia on esophageal biopsies and/or need of fundoplication and/or need of jejunal feeding	NA	NA
Castilloux et al (33)	45	0.5–18 y (median: 7.3)	20% 13%	Regurgitation Pyrosis	31% (histo)	44%
Sistonen et al (34)	101	21–56 y (mean: 36)	34%	Clinical symptoms	8% (25% histo)	10%
Catalano et al (22)	22	3–40 mo (median: 15)	45.5% (acidic)	Impedance-pH-metry	NA	0%
Legrand et al (18)	81 type C	9.5–18.5 y (mean: 13.3)	35%	Heartburn/regurgitation and/or pH-metry, endoscopy	NA	39%
Pedersen et al (25)	59	5–15 y (mean: 10.2)	56% 55%	Clinical symptoms pH-metry	49% (44% histo)	NA
Shah et al (26)	110	6 ± 3.5 y	39%	Symptoms ± pH-impedancemetry ± endoscopy	40% histo	17%
Bouguermouh and Salem (50)	45	3 mo–10 y	49%	NA	NA	18%

EA = esophageal atresia; GER = gastroesophageal reflux; NA = not available.

Although the panel recognizes that currently no controlled studies have been reported to show benefit of systematic acid suppression in EA patients, due to the high prevalence of GER in this cohort and the potential for GER-associated complications, the panel recommends that GER should be systematically treated with acid suppression in all patients with EA starting in the neonatal period. Long-term safety of proton pump inhibitor (PPI) in this population has, however, not been extensively studied, and concerns on consequences of acid suppression on microbiota and possible higher risk for GI and respiratory infections have recently been highlighted.

Statement 1: It is recommended that GER be treated with acid suppression in all EA patients in the neonatal period.

Expert opinion.
Low level of evidence
VOTES: 8/7/9/9/8/7 Accepted

2. How should GER be managed? (Fig. 1, box 2; Fig. 2, boxes 7 and 10)

Most of the complications due to GER in EA are related to acid (peptic esophagitis, Barrett esophagus, AS). There are no controlled trials on the medical management of GER in patients with EA. Although the quality of literature regarding the use of antireflux medication in children with EA is extremely poor (16), medical management of GER with PPIs and H2 receptor antagonists has been reported to be successful by reducing GI and/or respiratory symptoms or by achieving demonstrable weight gain (16). Due to their superior acid-blocking abilities, PPIs are recommended as the first-line therapy for acid-related gastroesophageal reflux disease (GERD) in children and for this reason are also recommended in the EA population (17). The benefit/risk ratio of long-term PPI treatment should be balanced in this population, and the need for prolonged use of PPIs should be reassessed regularly (see statement 6).

Statement 2: PPIs should be the first-line therapy for GER/GERD.

Expert opinion
Low level of evidence
VOTES: 9/9/9/8/9/9 Accepted

3. How long GER should be treated? (Fig. 1, boxes 2 and 4)

No prospective controlled studies have been performed to determine the optimal duration of acid suppression in infants, children, adolescents, or adults with EA. GER is common during infancy but can persist long term (Table 2). Complications due to GER occur mostly during the first year of life (AS, esophagitis, cyanotic spells, pulmonary problems, failure to thrive), but can also be observed later. A recent study showed that GERD tended to be more prevalent after 1 year of age (43%) compared with before (34%), and significant complications could develop after the 1 year of age even in children who were previously asymptomatic (4). GERD is one of the factors contributing to failure to thrive in infancy (18). The prevalence of peptic esophagitis is high throughout childhood and adulthood (Table 2).

Barrett esophagus is a long-term complication of EA (11,19). GERD also contributes to dysphagia in EA patients (12) and can negatively influence quality of life (QoL) (18,20). Hence, persistence of GER should be assessed by regular monitoring (see statement 6).

Statement 3: It is recommended that GER be systematically treated for prevention of peptic complications and anastomotic stricture up to the first year of life or longer, depending on persistence of GERD.

Expert opinion
Low level of evidence
VOTES: 8/7/8/7/9/7 Accepted

4. What is the role of 24-hour pH- and pH-impedance monitoring in EA patients? (Fig. 1, box 3; Fig. 2, box 8)

The gold-standard tests for the diagnosis of GERD are currently pH probe testing, pH- impedance testing, and wireless pH testing, all of which measure esophageal reflux burden (17). Twenty four-hour pH monitoring quantifies the esophageal acid burden, which is highly correlated with peptic esophagitis. pH-impedance (pH-MII) monitoring allows the evaluation of retrograde bolus movements in the esophagus independent of the pH, identifying nonacid reflux in the postprandial period and in patients receiving acid-suppressing therapy (21,22). The main use of pH-impedance monitoring is not to diagnose pathologic reflux but rather to try to correlate extra-esophageal symptoms with reflux events. One of the limitations of pH-impedance testing in patients with esophagitis or motility disorders (both of which are commonly found in patients with EA) is that baseline impedances are 75% lower than control patients (23).

Because of these low baselines, the software often fails to detect reflux events, so manual analysis, in addition to automated analysis, is critical to avoid underreporting of reflux. Experience with pH-impedancemetry is increasing in patients with EA showing that reflux events are equally as likely to be due to nonacid reflux as acid reflux in these patients (22–26). Since there are currently no medications that are effective in treating non-acid reflux, there is no practical therapeutic consequence of demonstrating nonacid reflux in patients with EA except consideration for fundoplication.

Statement 4a: pH monitoring is useful in evaluating the severity and symptom association of acid reflux in patients with EA.

Expert opinion
High level of evidence
VOTES: 7/9/9/9/8/8 Accepted

Statement 4b: pH-impedance monitoring is useful to evaluate and correlate non-acid reflux with symptoms in selected patients (symptomatic on PPI, on continuous feeding, with extra-digestive symptoms, ALTE, GER symptoms with normal pH-probe and endoscopy).

Expert opinion
Low level of evidence
VOTES: 7/8/9/9/9/7 Accepted

5. What is the role of esophagoscopy in EA patients? (Fig. 1, boxes 3 and 11; Fig. 2, box 5; Fig. 3, box 2)

In a retrospective study of the results of esophageal biopsies performed during routine esophagoscopy in children with EA, 80% of patients demonstrated moderate or severe esophagitis or gastric metapalasia at any time of follow-up (27). This study however does not mention whether the patients were on any PPI therapy at time of endoscopy. Multilevel esophageal biopsies are recommended for screening for peptic and eosinophilic esophagitis. The number of biopsies should be increased in the presence of macroscopic abnormalities or for screening for Barrett esophagus (at least 4 biopsies in each quadrant 1 cm above the Z line). Endoscopy is also useful in children post fundoplication because the recurrence of GER and peptic esophagitis is possible (11,28,29).

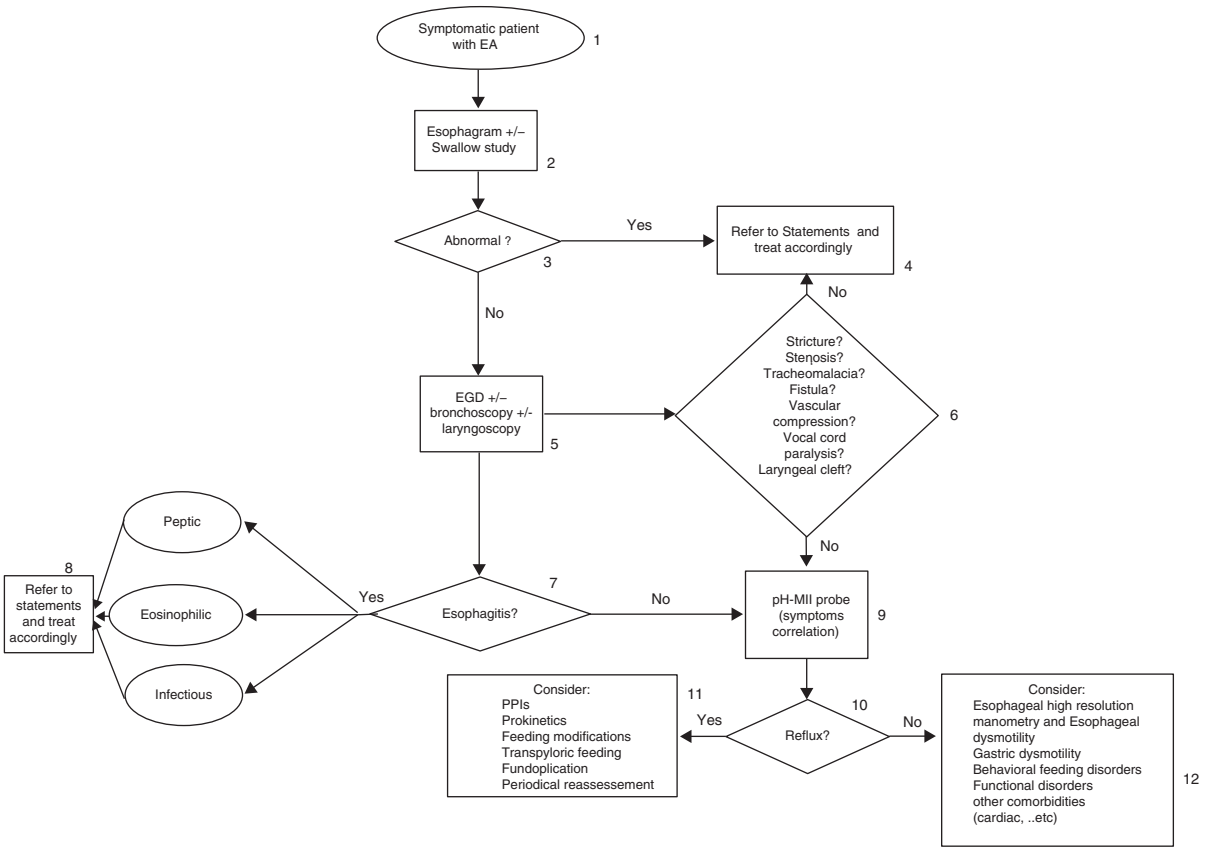

FIGURE 2. Algorithm for the evaluation and treatment of a symptomatic patient after surgical correction of an esophageal atresia.

Statement 5: Endoscopy with biopsies is mandatory for routine monitoring of GERD in patients with EA.

Expert opinion
High level of evidence
VOTES: 7/9/9/9/9/9 Accepted

6. How should GER be monitored, and when? (Fig. 1, boxes 3, 9 and 11; Fig. 2, box 8; Fig. 3, boxes 7 and 10)

GER remains frequent in EA children after the age of 2 years, even in asymptomatic patients, and can persist lifelong (Table 2). Complications due to GERD can be observed during childhood, adolescence, and adulthood and may include late or recurrent anastomotic stenosis, esophagitis, dysphagia, Barrett esophagus, and pulmonary complications (Table 2). Therefore, the panel recommends monitoring acid reflux at time of discontinuation of anti-acid treatment even is asymptomatic children, to confirm the absence of acid reflux, or conversely, the persistence of reflux and the need to continue treatment.

Statement 6: All EA patients (including asymptomatic patients) should undergo monitoring of GER (impedance/pH-metry and/or endoscopy) at time of discontinuation of anti-acid treatment and during long-term follow-up.

Expert opinion
High level of evidence
VOTE: 8/9/9/9/9/9 Accepted

7. How often do EA patients need surveillance endoscopy in childhood and adolescence? (Fig. 1, box 11)

No studies show benefit of routine upper GI endoscopy in the follow-up of EA patients. GER can, however, be asymptomatic and several studies have shown the absence of correlation between symptoms and esophagitis in this population (30,26,31–34). Esophageal mucosal abnormalities can be observed in up to 35% of EA patients at endoscopy despite the absence of symptoms (33,34), making the recommendation of endoscopic assessment based solely on symptomatology inappropriate. The goal of surveillance biopsies is to detect early esophagitis (with the opportunity for subsequent intervention) before the development of late complications of strictures, Barrett esophagus, and cancer.

Statement 7: Routine endoscopy in asymptomatic EA patients is recommended. The expert panel recommends 3 endoscopies throughout childhood (1 after stopping PPI therapy, 1 before the age of 10 years, and 1 at transition to adulthood).

Expert opinion
Low level of evidence
VOTES: 9/7/9/8/7/8 Accepted

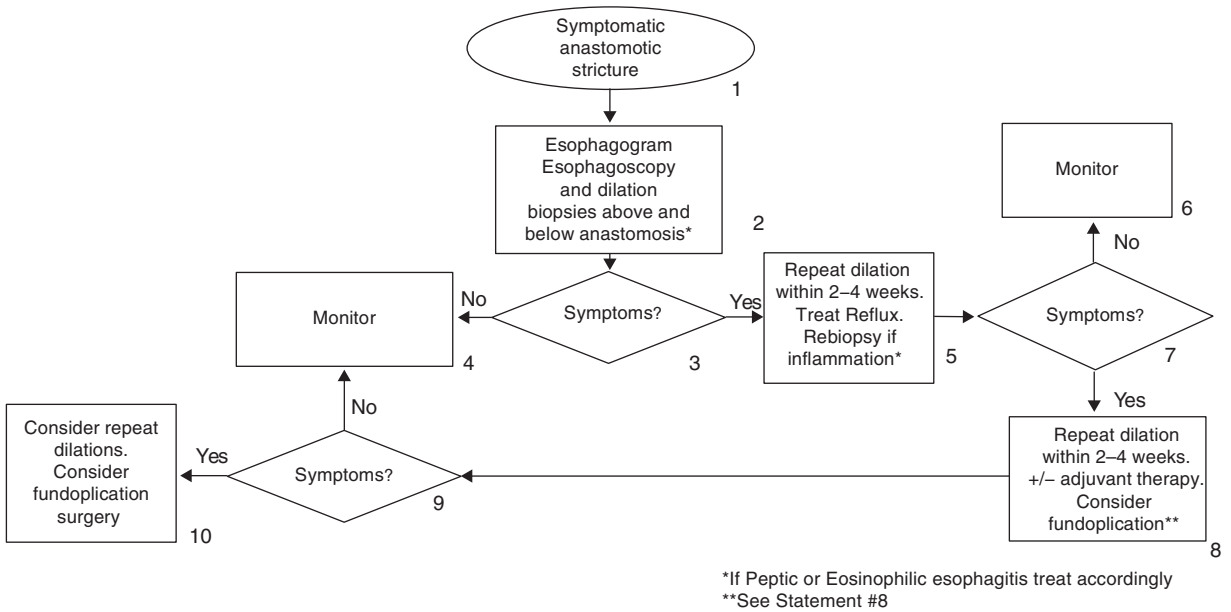

FIGURE 3. Algorithm for the evaluation and treatment of a symptomatic patient with an anastomotic stricture.

8. What is the role of fundoplication in EA patients with GER? (Fig. 1, box 5; Fig. 2, box 10, Fig. 3, boxes 8 and 11)

No controlled trial has been reported regarding the role of surgical management of GER in patients with EA. Cumulative risk of having a fundoplication performed in children with EA ranges from 0 to 45% (Table 2). In long-gap (LG) EA, GER is particularly frequent and severe, and leads to a high risk of AS, suggesting that fundoplication should be considered in a large proportion of these children (35–37). Several studies in non-EA patients report that fundoplication does not consistently reduce the risk of aspiration pneumonia, and respiratory admissions and may, in fact, increase the risk (38–41). In patients with EA who have poor motility and esophageal clearance, fundoplication may even worsen esophageal stasis by preventing gravity-driven esophageal clearance which may, in turn, worsen respiratory symptoms so the decision to proceed with fundoplication for respiratory symptoms alone, should be made with caution.

In a recent systematic review on the management of GER in EA patients, reasons stated for the need for antireflux surgery included failure of maximum conservative therapy for GER, failure to thrive, acute life-threatening event, esophagitis and a recurrent anastomotic stenosis.

Statement 8: Severe esophageal dysmotility predisposes EA patients to post-fundoplication complications. However, EA patients may benefit from fundoplication in: 8a: Recurrent anastomotic strictures, especially in long-gap EA.

Expert opinion
High level of evidence
VOTES: 8/9/8/9/8/9 Accepted

8b: Poorly controlled GERD despite maximal PPI therapy.

Expert opinion
High level of evidence
VOTES: 7/9/7/9/9/7 Accepted

8c: Long-term dependency on trans-pyloric feeding.

Expert opinion
Very low level of evidence
VOTES: 7/9/9/9/7/7 Accepted

8d: Cyanotic spells.

Expert opinion
Very low level of evidence
VOTES: 6/7/6/9/7/7 Accepted

9. What evaluations should be performed before fundoplication?

The preoperative evaluation should include reflux testing (24-hour pH-metry or pH-MII testing), upper GI series and endoscopy (42). pH-metry is required to confirm and quantify acid reflux; barium contrast study allows the diagnosis of hiatal hernia, associated congenital stenosis, the assessment of the anatomy of the cardiac region, and exclusion of other intestinal malformations. Endoscopy is required because it allows macroscopic evaluation and biopsies of the esophageal mucosa, for screening for peptic esophagitis and esosinophilic esophagitis or Barrett esophagus. To date, esophageal manometry, pH-metry and pH-impedancemetry have not been shown to be predictive for determining the risk of postoperative dysphagia (43,44). No data exist on the predictive value of high-resolution esophageal manometry for the occurrence of postfundoplication complications in EA patients.

Statement 9: Barium-contrast study, endoscopy with biopsies and pH-metry should at least be performed before fundoplication.

Expert opinion
High level of evidence
VOTES: 9/9/9/7/8/9 Accepted

10. What extra-esophageal manifestations of reflux and dysmotility are seen in EA patients? (Fig. 1, boxes 8 and 13; Fig. 2, box 1; Fig. 3, boxes 1, 3, 7 and 9)

Extra-esophageal symptoms are common in children, and adults with EA and these symptoms are associated with significant morbidity, especially in childhood (4,12,45–50). A total of 14% to 40% of patients have pulmonary symptoms which include cough in 8% to 75% of patients (18,47,48), wheezing in 14% to 40% (47,48), dyspnea in 37% (18), bronchitis in 14% to 74% (18,46,47), recurrent infections in 10% to 53% (50,51), bronchiectasis in up to 17% (12), restrictive lung disease in 11% to 69% (12,18), obstructive lung disease 38% to 50% (12,18), tracheomalacia in 14% to 29% (12,33) and pneumonia in 5% to 50% (46,47).

The GI causes of pulmonary symptoms are variable and include aspiration due to mucus or food retention in the proximal pouch or distal esophagus, AS, impaired esophageal motility, CES, aspiration during swallowing, GER, recurrent or missed fistulae, eosinophilic esophagitis, and esophageal pooling over a fundoplication. Aspiration of retained food or mucus above or below the anastomosis may occur because of stricture, or dysmotility possibly related to abnormal innervation to the proximal pouch or distal esophagus (52,53).

Non-GI causes also include vocal cord paralysis, laryngeal clefts, vascular rings and aspiration during swallowing (54). No study has systematically evaluated respiratory symptoms in children to determine the frequency of GI etiology for pulmonary symptoms. Additionally, no study has determined the impact of dysmotility, independent of reflux, on respiratory symptoms.

Statement 10: Symptoms of aspiration during swallowing may be identical to GER symptoms in young children.

Expert opinion
Low level of evidence
VOTES: 8/8/8/9/9/9 Accepted

11. How should clinicians investigate extra-esophageal manifestations in EA patients? (Fig. 2)

Multidisciplinary care of children with EA is critical and should include gastroenterology, pulmonary and otolaryngology specialists. Upper GI barium imaging is helpful in delineating recurrent or missed fistulae, AS and size of the upper pouch, congenital stenosis and esophageal extrinsic compression by a vascular ring. The diagnostic evaluation of aspiration during swallowing is important to pursue as 47% of children with EA have direct aspiration or penetration (54). Diagnostic testing includes modified barium swallow (videofluoroscopic swallow studies) or fiber optic endoscopic evaluation of swallowing, both of which assess swallow function (54). No study compares the sensitivity of these tests in the EA population, although 1 adult study suggests the techniques are comparable (55). If aspiration is identified during swallowing, the differential diagnosis must include developmental delay in swallowing function, neurologic etiology including Chiari malformations, hyper- or hypotonia, laryngeal clefts, and/or vocal cord paralysis. Studies of patients with EA suggest that 3% to 17% have clinically significant vocal cord paralysis and, while the incidence of laryngeal cleft in patients with EA is not known, 27% of patients with laryngeal cleft have EA (56–59). Therefore, diagnostic evaluation of the larynx and vocal cord evaluation by an otolaryngologist should be included. A rigid bronchoscopy by a pulmonologist, otolaryngologist, or surgeon should also be carried out to rule out a recurrent or missed fistula and to evaluate the degree of tracheomalacia.

GER is commonly implicated in extra-esophageal symptoms since 52% to 68% of coughs are associated with reflux events, and 25% to 50% of these are associated with non-acid episodes, particularly in children <1 (22). In another study, 39% of coughs were associated with reflux, with non-acid reflux correlating to a greater extent than acid reflux (23). pH impedancemetry may have a role in the evaluation of extra-esophageal symptoms thought to be secondary to GERD before considering fundoplication.

Statement 11a Patients with EA should be evaluated regularly by a multidisciplinary team including pulmonology and otolaryngology, even in the absence of symptoms.

Expert opinion
Low level of evidence
VOTES: 9/9/9/9/9/9 Accepted

Statement 11b Anatomic abnormalities (laryngeal cleft, vocal cord paralysis, missed or recurrent fistulae, anastomotic stricture, congenital stenosis, vascular ring) should be ruled out in EA patients with respiratory symptoms.

Expert opinion
High level of evidence
VOTES: 9/9/9/9/9/9 Accepted

Statement 11c If pH-metry or pH-MII is performed, symptom correlation during reflux testing, rather than total reflux burden is the most important indicator of reflux-associated symptoms.

Expert opinion
Very low level of evidence
VOTES: 9/6/9/7/7/8 Accepted

12. How should clinicians treat extra-esophageal manifestations in EA patients? (Fig. 2)

Little data and no controlled trials exist regarding the management of extra-esophageal symptoms in patients with EA. Hence, data available from the literature in children without EA on the treatment of extra-esophageal symptoms need to be extrapolated. In large well-designed randomized controlled trials in both adult and pediatrics, PPIs have failed to improve respiratory symptoms, reduce steroid and bronchodilator medication use, reduce emergency room visits, or improve QoL in patients with asthma and

other chronic lung diseases (60–62). Furthermore, in randomized controlled studies and case-control studies in adults with chronic lung disease, prolonged acid suppression use has been associated with an increased risk of respiratory infections (pneumonia, upper respiratory tract infections, pharyngitis), which may exacerbate the underlying lung disease (60,63–65). These data may not be relevant to children and adults with EA, who are likely at higher risk of reflux-related symptoms than patients with other respiratory conditions. Therefore, acid suppression, while helpful for preventing and healing esophagitis, should be used with caution for the sole treatment of extra-esophageal symptoms.

Fundoplication is frequently proposed for the treatment of extra-esophageal symptoms in patients with EA but currently no studies compare fundoplication to alternative therapies for the treatment of extra-esophageal symptoms in EA patients. More studies are needed to determine the impact of acid suppression, fundoplication and transpyloric feeding on extra-esophageal symptoms.

Statement 12: Acid suppression should be used with caution in patients with extra-esophageal manifestations of reflux.

Expert opinion
Low level of evidence
VOTES: 8/7/6/8/7/5 Accepted

13. How should ''Cyanotic spells'' be investigated and managed in EA patients? (Fig. 2)

The differential diagnosis for cyanotic spells in EA patients includes airway collapse from tracheomalacia, direct oral aspiration, esophageal dysmotility resulting in dysphagia, recurrent TEF, GER related reflux aspiration and events related to associated anomalies such as cardiac events. Anatomic issues such as AS, recurrent or missed fistulae, CES, vascular rings and laryngeal clefts need to be excluded. As no data provides information regarding how frequently ALTE is due to direct oral aspiration or GER related reflux aspiration, no child should undergo fundoplication for ALTE without prior assessment of swallowing function (54). Evaluation of children with ALTE must include a multidisciplinary team of surgeons, gastroenterologists, pulmonologists and otolaryngologists to ensure that a full differential diagnosis is considered.

The studies of ALTE in EA consist of retrospective case series in which different surgical management approaches were taken with subsequent reviews of the outcomes (66). Management includes aortopexy (67), fundoplication, conversion from gastrostomy feeding to transpyloric feeding, tracheostomy placement, and maximization of medical therapy for reflux disease.

The treatment of direct oral aspiration involves feeding modification. Current literature is focused on the surgical management of ALTE, and no studies focus on the medical management (medications, change in feeding methods etc) of cyanotic spells or ALTE in this population. No prospective, controlled studies compare diagnostic algorithms or therapeutic outcomes for patients with ALTE.

Statement 13a: The etiology of life-threatening events is multifactorial and merits a multidisciplinary diagnostic evaluation before surgical intervention.

Expert opinion
Very low level of evidence
VOTES: 9/9/9/9/9/9 Accepted

Statement 13b: Anatomic issues (strictures, recurrent or missed fistulae, congenital esophageal stenosis, vascular rings, laryngeal clefts) and aspiration need to be excluded in children with ALTE.

Expert opinion
Low level of evidence
VOTES: 9/9/9/9/9/9 Accepted

• Dysphagia and esophageal function in EA

Based on ten series of patients reported for the past 3 decades, the incidence of dysphagia in infants, children and adolescents with EA after surgical repair ranges between 21% and 84% (19,51,68–72). Dysphagia is estimated to be more prevalent than reported in the literature, particularly as children may not recognize their symptoms as abnormal and may appear better adapted to their unique situation (72). Children and adolescents with EA continue to experience dysphagia regardless of the number of years after surgical repair. In a series of 69 patients with EA, 45% had dysphagia at 5 years, 39% at 5 to 10 years, and 48% at greater than 10 years (51).

In children with EA, the etiology of dysphagia may include inflammatory or anatomic causes such as peptic esophagitis, eosinophilic esophagitis (75), AS (19,68–70), congenital stenosis (76), peptic stricture, post-fundoplication obstruction, vascular anomalies (77), anastomotic diverticulum (19,73), mucosal bridge (78,79) and inlet patch (80). In the absence of the latter causes, esophageal dysmotility remains the accepted explanation.

Esophageal motility can be assessed by either contrast study, esophageal manometry (either water perfused or high-resolution solid state) or videofluoroscopy (74). The patterns of esophageal dysmotility in a cohort of children with EA were recently described using high-resolution manometry and were reported abnormal in all patients, with 3 types of abnormalities observed: pressurization (15%), isolated distal contractions (50%) and aperistalsis (35%) (72). Consistently, the pattern of esophageal dysmotility was not predictive of the presence or severity of dysphagia. GER-related symptoms are prominent in patients with aperistaltic esophagus (72,81). No prospective longitudinal studies of patients with EA document the natural history of esophageal dysmotility and the correlation between symptoms and dysmotility.

The underlying cause of the dysmotility remains unclear and controversial. In EA-operated patients, it has been postulated that dysmotility may be caused either by intrinsic factors related to abnormal development of the esophagus (53,82,83) or by operative maneuvers responsible for a partial denervation. Postoperative complications (including leaks, anastomotic stenosis, and subsequent esophageal dilations) could also cause local trauma and inflammation leading to further neuronal and muscular damage. Recently, high-resolution esophageal manometry was found to be severely affected in 2 children with isolated TEF studied before surgical repair suggesting that esophageal dysmotility is congenital in nature rather than secondary to surgical intervention (84).

14. When should dysphagia be considered in patients with in EA?

Dysphagia in children with EA can present with simply a complaint of difficulty in swallowing (50%), nausea (27%), epigastric burning (21%), heartburn (14%-50%), postprandial fullness (14%), early satiety (14%), eructation (14%), regurgitation (7%-50%), or epigastric pain (7%) (69). Choking is reported in 10% of patients at 5 years, 4% at 5 to 10 years, and 7% at greater than 10

years after surgical repair (51). Most patients cope with the symptoms and have adapted and consider these symptoms as minor problems (73). Odynophagia with discomfort or pain with propagation of the food bolus is also reported (74). Children may have minor or occasional difficulties with swallowing, may eat slowly or drink excessive amounts of liquids with foods, or develop food impaction (68,72). Significant changes in eating habits are reported in up to 73% of patients with dysphagia (need to drink, change in diet, last to finish meal) (72).

Statement 14: Dysphagia should be suspected in patients with EA who present with food aversion, food impaction, difficulty in swallowing, odynophagia, choking, cough, pneumonia, alteration in eating habits, vomiting, and malnutrition.

Expert opinion
Low level of evidence
VOTES: 9/9/9/8/8/9 Accepted

15. How should dysphagia be investigated in EA patients? (Fig. 2)

Evaluation of dysphagia should begin with contrast studies that can be helpful in identifying a structural etiology for dysphagia. Esophagography after EA repair should be performed because of the high index of suspicion for the presence of distal congenital esophageal stricture (CES), since the diagnosis and adequate management of CES can often be delayed (76,85). Endoscopy with biopsies allows the evaluation of the anastomosis (stricture, diverticulum), the esophageal mucosa (peptic, eosinophilic or infectious esophagitis) and the diagnosis of congenital stenosis, mucosal bridge, inlet patch or extrinsic compression (vascular anomalies, tight fundoplication wrap). In children with EA, dysphagia has low correlation with mucosal esophageal inflammation (33). High-resolution esophageal manometry ideally with impedance is also recommended for the investigation of dysphagia in EA patients who have a normal esophagogram and endoscopy with biopsy.

Statement 15: We recommend that all EA patients with dysphagia undergo evaluation with upper GI contrast study and esophagoscopy with biopsies.

Expert opinion
Low level of evidence
VOTES: 8/7/9/9/9/9 Accepted

16. What is the role of esophageal manometry in EA patients with dysphagia? (Fig. 2, box 12)

Esophageal motility testing is useful in patients with EA and dysphagia in whom esophageal stricturing has already been addressed. It is important to classify and categorize the pattern of esophageal dysmotility with esophageal manometry and to correlate the degree of dysmotility with bolus transit (when performed with impedance). The esophageal dysmotility seen in manometry, however, may not result in changes in medical management because the correlation between dysphagia, motility abnormalities, and bolus transit is imperfect.

Statement 16: Esophageal manometry is useful to characterize esophageal motility patterns in EA patients with dysphagia. However, the impact on clinical outcome has yet to be determined.

Expert opinion
Low level of evidence
VOTES: 7/8/8/8/9/9 Accepted

17. How should dysphagia be managed in EA patients? (Fig. 2, box 12)

The management of dysphagia must be conducted according to the underlying cause. There is no controlled study on specific treatments of dysphagia in patients with EA. Treatment options may include but not limited to:

- Feeding adaptation
- Treatment of esophagitis (peptic, eosinophilic, or infectious) and inlet patch
- Prokinetics
- Treatment of stricture, stenosis, mucosal bridge, or anastomotic diverticulum
- Surgical repair of vascular anomaly
- Gastrostomy tube feeding
- Esophageal replacement
- Dilation of fundoplication

Statement 17: We recommend tailoring management of dysphagia to the underlying mechanisms.

Expert opinion
Very low level of evidence
VOTES: 8/8/9/9/9/9 Accepted

18. How should dysphagia in EA patients post-fundoplication be investigated?

Dysphagia is a frequent complication after fundoplication in the general population but is more frequent in patients operated at birth for EA. In a series of 148 children who underwent fundoplication (87 of whom had EA), dysphagia and/or stenosis occurred in 17.2% of EA patients versus 6.5% of other children (29). In another study it has been reported to be 31% (42). In a small series of 14 EA patients who underwent fundoplication, 7 of them developed severe dysphagia requiring feeding gastrostomy (86). In the series by Levin et al, postoperative dysphagia occurred in 45% and 38% of children post partial or total fundoplication respectively (87). Post-fundoplication dysphagia could be secondary to the combination of reduced esophageal motility and a tight wrap, outflow obstruction at the wrap level or as a result of herniated wrap or paraesophageal hernia. Esophagoscopy with biopsies to exclude reflux recurrence with esophagitis may also be useful. In young children, post-fundoplication dumping syndrome is a differential diagnosis and must be ruled out because symptoms (feeding difficulties and postprandial discomfort) may be interpreted as dysphagia.

In evaluating dysphagia, contrast studies should be used to assess for anatomic/structural etiology. Post-fundoplication dysphagia should be evaluated by administering contrast orally or via a nasoesophageal tube to assess for flow resistance at the level of the fundoplication wrap. Since dysphagia may be related to etiologies other than the fundoplication, endoscopy with biopsies is necessary for evaluation of the anastomosis (stricture, diverticulum), and the esophageal mucosa (peptic, eosinophilic, or infectious esophagitis).

Endoscopy may demonstrate the tight wrap (and allow for wrap dilation), though there are no data comparing endoscopic appearance of the wrap to radiological imaging. To assess for the degree to which the fundoplication may contribute to esophageal obstruction, a high-resolution esophageal motility study (combined with impedance) may be used to demonstrate not only fundoplication pressures, but also impaired bolus clearance and elevated intra-bolus pressures. However, there are no prospective studies documenting the effect of results high-resolution manometry on outcomes in EA patients following anti-reflux surgery

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Statement 18: In EA patients with post-fundoplication dysphagia, we recommend a contrast study to rule out mechanical complications, EGD with biopsy and, if inconclusive, high-resolution manometry ± impedance.

Expert opinion
Very low level of evidence
VOTES: 9/9/9/8/9/9 Accepted

19. How should dysphagia in EA patients post-fundoplication be managed?

The management of post-fundoplication dysphagia needs to reflect the underlying cause. There are no controlled studies on specific treatments of post-fundoplication dysphagia in patients with EA. Treatment options may include but not limited to:

- Feeding adaptation
- Treatment of esophagitis (peptic, eosinophilic or infectious)
- Prokinetics
- Balloon dilation of the wrap
- Botulinum toxin to the LES
- Gastrostomy tube feeding
- Surgical revision of fundoplication
- Gastrostomy
- Esophageal replacement

Statement 19: We recommend tailoring management of post-fundoplication dysphagia to the underlying mechanism(s).

Expert opinion
Very low level of evidence
VOTES: 8/9/8/9/8/7 Accepted

20. When should we look for associated vascular abnormalities in EA? (Fig. 2, box 6)

In a series of 76 children born with EA/TEF, vascular abnormalities were reported in 18% of children. The most common abnormalities were an aberrant right subclavian artery (ARSA) in 12% (9/76) and right-sided aortic arch in 6% (5/76) (77). LG EA and severe cardiac malformations requiring surgery are both significantly associated with vascular anomalies. Often asymptomatic from a GI perspective, these abnormalities may be the cause of respiratory symptoms (dyspnea, cough, cyanosis) and/or exacerbate GI symptoms (dysphagia) when a ring completely or incompletely encircles the trachea and/or the esophagus, resulting in extrinsic compression. Severe complications, such as massive GI bleeding secondary to an ARSA-esophageal fistula related to a stent placement after EA repair due to an ARSA which was not recognized before stent placement, have been reported (88). A similar phenomenon has been reported after prolonged (>17 days) placement of a nasogastric tube in children without EA (89). Since an ARSA is not visible during esophageal surgery, and since the diagnostic yield of routinely used techniques (preoperative cardiac ultrasound and esophagram) have low sensitivity and negative predictive value for the diagnosis of ARSA, Computerized Tomographic (CT) angiography or chest magnetic resonance imaging (MRI) should be performed to rule out such malformations before placement of a stent or long-term nasogatric tube, or in patients with unexplained respiratory symptoms.

Statement 20: Even though congenital vascular malformations are usually asymptomatic, they may be the underlying etiology for dysphagia, dyspnea, or cyanosis, by causing external compression on the esophagus and/or trachea. We recommend that congenital vascular malformations be excluded in these situations by chest CT or MR angiography.

Expert opinion
Low level of evidence
VOTES: 9/8/9/9/7/9 Accepted

• Feeding and nutrition in EA patients

The causes of feeding difficulties in children with EA are multifactorial and include oropharyngeal, esophageal, and behavioral disorders. No prospective controlled studies describe abnormal feeding behaviors in children with EA. All studies currently rely on recollection of historical details by questionnaire or chart reviews. Koivusalo et al, reported that 94% of 130 EA patients followed up long term were doing well with oral feeds (90). In another study, Khan et al found that there was no difference in the achievement of feeding milestones in children with EA compared with controls (91). In a study of 124 patients by Puntis et al, patients with EA had solid foods introduced at a mean age of 12 months versus 4 months in control group ($P = 0.003$) (92). Difficulties in feeding can result in added stress in the family unit (93). The causes of feeding difficulties include aspiration, dysmotility, esophageal outlet obstruction, esophageal inflammation, and AS. GER has also been implicated as a cause for feeding difficulties although no data support the fact that patients with EA and GER have worse feeding outcomes than patients without reflux.

Fundoplication, which can create a functional esophageal outlet obstruction in the context of dysmotility, can also cause dysphagia and feeding difficulties in children with EA (29). No studies address the impact of fundoplication on acquisition of feeding milestones or rates of significant food impaction.

Aspiration is an underrecognized cause of feeding difficulty in children with EA. In a case series of patients with laryngeal cleft, many of whom had EA, 18% of patients had feeding difficulties, 4.5% had choking and 4.5% had dysphagia (58). Smith et al describe a case series in which 61% of all EA patients had coughing during eating, and this, combined with the reports of aspiration during eating, suggests that all of these issues may contribute to dysfunctional eating patterns (94). Furthermore, respiratory distress of any nature may predispose patients to feeding difficulties (95,96). Finally, patients may develop a fear of eating or texture aversion(s) related to a history of choking on food. Khan et al reported 23% of patients have a history of food impaction which

may result in limitation in intake of certain foods, and which result in feeding behaviors that differ from control patients (91).

21. How should abnormal feeding behaviors in EA be prevented and managed?

Neither retrospective nor prospective studies address how to prevent or treat abnormal feeding behaviors in children with EA. In infants before EA repair, case reports of successful sham feeding, when babies are fed small volume feeds which are immediately suctioned from the esophageal pouch, but the studies are limited by their methodologies (97). Prospective studies documenting the type of feeding difficulties, and the outcomes of standardized interventions in children with EA are needed.

Statement 21: No data are available on the most efficacious methods of avoiding feeding disorders in children with EA. However, the committee recommends a multidisciplinary approach to prevent and treat feeding difficulties.

Expert opinion
Very low level of evidence
VOTES: 9/8/8/9/9/9

22. Is there a risk of malnutrition in infants, children, and adolescents with EA?

Nutritional outcome studies are limited by a lack of adjustment for comorbidities (cardiac, genetic, neurologic), which may have a large impact on growth. Puntis et al found that while mean heights and weights (mean height z score -1.78 ± 1.7) and mean weight for height (-1.1 ± 0.9) were lower in children with EA compared with controls ($P < 0.0001$), no correlation was found between feeding scores and growth parameters (92). A study of 371 patients by Deurloo et al, found that long term, only 7% of patients were less than the 5th percentile for height and weight. A history of GER and low birth weight were both predictors of reduced growth (14). A retrospective study of 81 type C EA patients with a mean age of 13.3 years, by Legrand et al reports that 75% had a normal BMI, 16% were obese and 9% were undernourished (18).

Statement 22: Intensive early enteral and oral nutrition intervention and advances in neonatal care and surgery have reduced the risk of long term malnutrition in children with EA; however, other associated comorbidities may increase this risk.

Expert opinion
Low level of evidence
VOTES: 9/9/8/9/9/9 Accepted

• Anastomotic stricture (Fig. 3)

AS has been reported to be the most frequent post-operative complication in EA, occurring in 18% to 60% of patients (2,4,98–101). Several factors contribute to the development of AS: long gap between the 2 esophageal pouches and consequent anastomotic tension, postoperative anastomotic leak (97,100), and GER (99,100,104). The presence of a long gap (LG) between the 2 esophageal ends is associated with a higher AS incidence, as reported by several authors (98,99,102–107). Lack of consensus regarding the gap definition, and how and when the gap length between the 2 esophageal ends should be measured, makes objective comparisons between publications and individual centers difficult. The EA gross types A and B, are characterized by an increased risk of stricture (108).

23. What is the definition of a clinically relevant anastomotic stricture in patients with EA? (Fig. 3, box 1)

AS is defined as a narrowing at the level of the esophageal anastomosis. The severity of esophageal narrowing does not correlate with symptoms. The panel suggests that an AS should be considered clinically relevant only in patients with symptoms, not in asymptomatic patients with relative anastomotic narrowing.

Statement 23: In addition to relative esophageal narrowing at the level of the anastomosis (by contrast and/or endoscopy), significant functional impairment and associated symptoms need to be present for anastamotic strictures to be considered clinically significant.

Expert opinion
No level of evidence
VOTES: 7/8/7/8/9/6 Accepted

24. When should anastomotic strictures in EA be diagnosed?

A variety of symptoms thought to be due to AS have been described in literature. These depend upon the age of the child and the type of food ingested (liquid versus solid). These symptoms are: feeding and swallowing difficulties, regurgitation and vomiting, mucus or food retention in the proximal pouch, cough, drooling, recurrent respiratory infections, foreign body impaction, and poor weight gain. AS should be suspected in presence of any of these symptoms. No studies indicate whether these symptoms alone are sensitive or specific enough to diagnose an AS.

Some groups have proposed aggressive systematic screening for AS and/or routine dilation(s) of the esophagus, even in the absence of symptoms, to prevent symptoms secondary to AS from developing (109–111). Koivusalo et al compared the effect of routine stricture dilation versus a ''wait-and-see approach'' and found no differences in the outcomes of the 2 groups in terms of dysphagia, nutritional status, and respiratory symptoms, suggesting that a ''wait-and-see approach'' that is less invasive for the patient may be superior to prophylactic dilations (111). Others recommend endoscopy or barium swallow ''on-demand'' in patients with symptoms suggestive of AS (99–101). No prospective controlled studies compare the 2 approaches.

Therefore, the panel suggests close follow-up of all EA patients in the first 2 years of life with special attention to symptoms suggestive of AS. Infants fed only with liquids, must be followed during introduction of solid food. Patients with LG EA and postoperative anastomotic leak (which are risk factors for developing AS) need close follow-up to avoid development of a severe/and sometimes complete anastomotic closure with a resultant high risk for aspiration and difficult-to-perform endoscopic dilations.

Statement 24: There is no evidence that routine screening and dilation is superior to evaluation and treatment in symptomatic patients. We recommend that AS be excluded in symptomatic children, and those children who are unable to achieve feeding milestones.

Expert opinion
Low level of evidence
VOTES: 8/7/7/9/8/8 Accepted

25. How should anastomotic stricture be diagnosed in EA? (Fig. 3, box 2)

No studies compare the diagnostic yield of endoscopy versus barium swallow for detection of AS after EA repair. Contrast radiographs allow evaluation of the esophageal morphology with possible diagnosis of associated CES and planning a patient-specific therapeutic strategy. Endoscopic evaluation offers the opportunity of combined diagnosis and treatment with dilation(s).

Statement 25: Diagnosis of anastomotic stricture can be done by either contrast study and/or endoscopically.

Expert opinion
No level of evidence
VOTES: 9/9/9/9/9/9 Accepted

26. How should anastomotic strictures be managed? (Fig. 3, box 2)

Anastomotic dilation is the first line of therapy for AS. The aim of dilation is to obtain an esophageal diameter that allows a normal, age-appropriate capacity for oral feeding, without respiratory or digestive symptoms. General anesthesia with tracheal intubation is recommended for airway protection during the procedure.

A guide wire inserted under endoscopic or x-ray control is helpful to avoid the risk of esophageal perforation by the dilator tip. x-Ray evaluation of guide wire passage and correct position in the gastric body should be done in case of difficult wire passage. No controlled studies compare hydrostatic balloon or a semi-rigid dilator for treatment of AS in EA patients. No evidence has been reported of increased effectiveness or safety for one or the other dilator type. The advantage of hydrostatic balloon dilators is the radial force applied on the stricture while avoiding axial forces (112). The inflating balloon device allows a standard force application. The balloon is filled with water or contrast medium. In the latter case, fluoroscopic control allows the monitoring of the disappearance of the waist in the balloon caused by the stricture (112). Persistence of the waist suggests that the procedure was only partially successful (113). The Savary-Gilliard semi-rigid dilator applies radial force on the stricture but also an axial one with stricture stretching, with may theoretically result in greater esophageal trauma (114). On the other hand, the experienced operator can apply the correct force with the semi-rigid dilator to obtain the desired dilation. Savary dilators are reusable after sterilization. Careful post-dilation endoscopic evaluation is recommended to check for possible perforation. Dilation must be carried out using the technique with which the operator is most skilled and experienced.

No controlled studies report on the optimal number of dilations and the optimal interval between dilation sessions for treatment of AS after EA repair. Different authors reported on varying intervals between dilations ranging from 7 days (109), 15 days (113), and 21 to 30 days. Others report a dilation session schedule based on the severity of the stricture and symptom relapse or recurrence (108,115). No consensus exists regarding the ideal interval between dilation sessions.

Statement 26a: We recommend that dilation be performed in children with EA under general anesthesia and tracheal intubation.

Expert opinion
High level of evidence
VOTES: 9/9/9/9/9/9 Accepted

Statement 26b: We recommend the use of a guide wire to insert the chosen dilator (balloon or semi-rigid) through the stricture under endoscopic or fluoroscopic control.

Expert opinion
No level of evidence
VOTES: 7/7/7/7/9/6 Accepted

27. What is the definition of recurrent anastomotic stricture in EA patients? (Fig. 3, boxes 8 and 10)

No evidence-based definition exists regarding the definition of recurrent AS in EA patients (116).

Statement 27: No evidence exists on the definition of recurrent anastomotic stricture in EA patients. Based on expert opinion we believe 3 or more clinically relevant stricture relapses constitutes recurrent stricture.

Expert opinion
No level of evidence
VOTES: 7/8/9/9/7/9

28. What adjuvant treatments are available in recurrent strictures in EA patients? (Fig. 3, box 8)

To prevent the recurrence of AS, different adjuvant treatments have been proposed, such as intralesional steroids, mitomycin C, stents, and endoscopic knife. These treatments have been reported in case reports or retrospective small case series, with extremely variable outcomes and definition of recurrence. Currently no controlled studies are, however, reported for any of these treatments for strictures in children with EA.

Corticosteroids. Use of intralesional triamcinolone acetonide injections has been reported, both in adults and children, with inconsistent improvement in AS (10,116–118). Potential complications of esophageal injection(s) of steroids include perforation, intramural infection, candida infection, mediastinitis, and pleural effusion, as well as the potential for adrenal suppression from exogenous systemic steroid administration. No side effects have been reported for both local or systemic short-term steroid treatment. Data on systemic steroids in AS are lacking.

Mitomycin C is an antineoplastic antibiotic with anti-fibrotic activities. It has been described to exert inconsistent results at different drug concentrations, when used as a topical agent applied to the AS after the dilation (119). In a retrospective study of 21 EA patients with recurrent AS, the authors reported similar results in eleven patients that underwent endoscopic dilations plus mitomycin C (0.1 mg/mL), and ten patients that received endoscopic dilations alone (79).

Stents. In a retrospective study, a fully covered metal stent was reported to be effective in 6/23 cases of AS (120). Another stent type, the ''dynamic'' custom stent, was reported to be effective in 21/26 patients with AS (121). Esophageal to ARSA fistula was reported as a major complication of esophageal stenting in EA patients (see statement 22) (88).

Endoscopic knife. AS section was reported in several patients as an adjuvant effective strategy in resistant and recurrent AS (122).

Statement 28: Potential adjuvant treatments for the management of recurrent strictures in EA patients may include intralesional and/or systemic steroids, topical application of mitomycin C, stents and an endoscopic knife.

Expert opinion
No level of evidence
VOTES: 8/9/8/9/9/9 Accepted

• Congenital stenosis in EA

29. How should congenital stenosis in EA be diagnosed? (Fig. 2, box 6)

CES is characterized by an intrinsic circumferential narrowing of the distal esophageal lumen that is present at birth, although it may not necessarily be symptomatic in the neonate. Incidence of CES in patients with EA is high, and has been reported to be present in between 3% and 47% of patients (76,123–127). In contrast, the incidence of CES is 1 in 25,000 to 50,000 live births in the general population (127). In patients with EA, CES may be suspected during the initial surgery (124), or afterward because of symptoms of dysphagia in patients without AS, or during routine anastomosis evaluation by barium swallow or endoscopy. Diagnosis of CES associated with EA is difficult, and treatment may be delayed. Therefore, in all children operated for EA, a high index of suspicion for associated CES is required, especially in the presence of dysphagia, food impaction, feeding difficulties, failure to thrive, respiratory symptoms, or AS. Esophagogram allows diagnosis of CES in the majority of patients. In a retrospective study, >1 radiological examination was, however, required, because the diagnosis of CES was either missed or misinterpreted as transient spasm, dysmotility, or esophageal narrowing due to reflux (76). Endoscopy confirms the diagnosis by revealing normal esophageal mucosa and esophageal narrowing distal to the anastomosis.

Three subtypes of CES are known: ectopic tracheobronchial remnants (TBRs) in the esophageal wall, segmental fibromuscolar hypertrophy (FMH) of the muscle and submucosal layers with fibrosis, and a membranous diaphragm (127). Conventional imaging tools as well as CT scan and magnetic resonance imaging cannot differentiate TBR from FMH (127). Endoscopic ultrasonography with miniprobes inserted through the operative channel of the standard gastroscope or by the side of a thin endoscope, allows the evaluation of the esophageal wall at level of CES, and can differentiate FMH from TBR subtypes (126,128–130).

Statement 29: In EA patients we recommend esophagram as the first step in suspected CES, and endoscopy to confirm the diagnosis and exclude other pathology.

Expert opinion
Low level of evidence
VOTES: 9/9/9/9/8/9 Accepted

30. How should congenital stenosis be managed in EA patients? (Fig. 3, box 6)

There is no consensus about treatment of CES. Conservative treatment involves endoscopic dilation(s) of CES with balloon or Savary dilator under general anesthesia. Dilation of CES is attempted as a first-step treatment in all patients in many series (76,123–126). In a series of 47 patients with CES, Romeo reported that conservative treatment was effective in 96% of cases, for both the tracheobronchial remnants or fibromuscular subtypes of CES (126). McCann (76) reported that 59% of patients were successfully treated with dilations. Because no technique has been shown to be superior to the other, the choice of dilation technique (bouginage or balloon dilator) depends on personal experience or preference of the operator.

Surgery is reserved for cases where dilations have failed (76), or in the presence of a diagnosis of tracheobronchial remnants (76,125,127,128). There is, however, no difference in outcome following dilation of the tracheobronchial remnants or fibromuscular subtypes of CES (126).

Esophageal perforation during dilation may occur in 3.4% to 18% of procedures, especially following treatment of the tracheobronchial remnant subtype (76,126,127).

Statement 30: We suggest endoscopic dilation as the first line of treatment in CES.

Expert opinion
Moderate level of evidence
VOTES: 9/9/9/7/9/8 Accepted

• Eosinophilic esophagitis (EoE) in EA

31. What is the impact of eosinophilic esophagitis on symptoms in EA patients? (Fig. 3, box 8)

There are no case-control studies on the prevalence of EoE in patients with EA. 48 cases of EoE in EA patients have been reported in literature (25,75,131–135). The largest reported number was in the study by Dhaliwal et al, which reported a 17% incidence in a retrospective review of biopsies taken from 103 EA patients for a 13-year period. This is greater than the reported incidence of EoE in the general pediatric population, of 1 in 10,000 children, and 8% to 10% in children with suspected GER refractory to antireflux treatment (136). The higher incidence of EoE in the EA cohort has been ascribed to a possible genetic association, impairment of esophageal mucosal barrier function by acid refluxate and prolonged exposure to acid suppressive medication (75). The majority of EA patients with EoE had type C EA in these studies. In the study by Dhaliwal et al 28% had LG EA and EA patients with LG had an 11.8 times relative risk of developing EoE in this study (75). As presenting symptoms of EoE are similar to those of GER, misdiagnosis or delayed diagnosis often occurs in EA (75). Compared to EA patients without EoE, EA patients with EoE had a significantly higher incidence of symptoms of vomiting, dysphagia, or cyanotic spells, and also had a significantly higher incidence of fundoplication and gastrostomy for feeding difficulties (75). In the study by Dhaliwal et al, 38% had a stricture at the time of diagnosis of EoE, and a significantly greater number of patients with EoE developed late strictures (>1 year of age) when compared with those without EoE (75). In this study, EA patients had a 1.9 times relative risk for stricture formation if they had EoE, LG, or both. The relative risk of EA patients with both LG and EoE developing strictures was 4:1 (75). A high prevalence of strictures has been reported in the other studies as well (131–134).

Statement 31: EoE needs to be excluded in EA patients of all ages with dysphagia, reflux symptoms, coughing,

choking, or recurrent strictures that are refractory to PPI, before proceeding to anti-reflux surgery.

Expert opinion
Low level of evidence
VOTES: 9/8/7/9/9/9 Accepted

32. How should EoE be diagnosed and managed in EA patients?

For a proper diagnosis of EoE, it is important to demonstrate hypereosinophilia (>15 eosinophils/high-powered field) in patients on high-dose acid suppression with PPIs. Multiple esophageal biopsies in keeping with standard guidelines for diagnosis of EoE, need to be taken during esophagoscopy, because EoE is described as a patchy disease process (136). Moreover, on endoscopy, the typical macroscopic findings of EoE—namely furrows and white exudates—may not be seen in all EA patients (75,131–133). There is no evidence that the treatment and management of EoE in EA patients should be different from other children.

Therefore, current recommendations for treatment of EoE in the general population should be followed in EA patients (137,138). The only study to look at outcomes post-treatment of EoE in EA patients was by Chan et al. They reported that for a median follow-up period of 23 months, treatment of EoE resulted in an improvement, not only in histology, with a significant reduction in the intraepithelial eosinophil count, but also in symptoms of dysphagia and reflux, prevalence of strictures, and need for dilations (139).

Statement 32: We recommend multiple esophageal biopsies, both proximal and distal to the anastomosis for the diagnosis of EoE. Management of EA patients with EoE should follow consensus recommendations for treatment of EoE in the general population.

Expert opinion
Low level of evidence
VOTES: 9/8/9/9/9/9 Accepted

• Associated gastrointestinal conditions in children with EA

Approximately 50% of EA patients have 1 or more other GI anomalies—mostly commonly part of which the VACTERL association (vertebral, anorectal malformations, cardiovascular, renal, and limb anomalies) (140). The incidence of GI anomalies, excluding anorectal malformations, in association with EA, varies from 3.6% to 7.5% (141).

Hypertrophic pyloric stenosis (HPS). HPS occurs in approximately 1 in 400 live births in the western population (142,143). The 7.5% incidence of HPS in EA patients reported by Van Beelan was 30 times higher than the 0.25% incidence of HPS in the normal population (143). The diagnosis was generally delayed, with a median of 6 days (range, 1–21 days) (144).

Malrotation. The reported incidence of malrotation in EA patients has ranged from 8.6- 12.7% (141). There is often a delay in diagnosis and there are reports of death due to volvulus (141). In EA patients, often only the anastomosis is imaged, as a result of which a malrotation can be missed. Upadhyay felt that contrast studies should include the duodenum to note the rotation of the bowel, and at the time gastrostomy is performed, along with searching for other atresias, one should look for malrotation of the small intestine (145).

Heterotopic gastric mucosa (HGM). A well-defined area of HGM or ''inlet patch,'' typically located in the proximal esophagus just inferior to the upper esophageal sphincter (146), has been reported in up to 34% of patients with EA (147) versus 0.1% to 10% in adults and up to 21% in children (146). HGM is typically considered a benign finding, but studies show that GI or respiratory complications can occur as a result of acid secretion from HGM (148). Symptoms described include mild dysphagia, GI bleeding, ulceration, fistula formation, strictures, malignancy, cough, wheezing, and asthma (149).

Duodenal atresia (DA)/duodenal stenosis (DS). The association of EA and DA/DS is well recognized, although uncommon (150,151). In babies with EA-TEF, the diagnosis of a coexisting duodenal obstructing lesion can usually be made on the basis of a plain radiographic study of the chest and abdomen, while in those with pure EA, the diagnosis may be subtler and may require the use of ultrasound or instillation of contrast material into a gastrostomy (152). Quite often, the DA/DS is not appreciated until esophageal continuity is established, or when gastrostomy feedings fail (153).

Heterotopic pancreas (HP). HP is defined as pancreatic tissue lacking anatomical and vascular continuity with the pancreatic gland, which is most often located along the greater curvature of the prepyloric antrum. A prospective case-control study in children with EA reported a significantly higher incidence of gastric HP in 18.7% of EA patients compared with 0.5% in the control group (154). None developed complications related to HP (154).

Dumping syndrome. Dumping syndrome can occur after primary anastomosis of EA without anti-reflux surgery (153). It can manifest as feed refusal, nausea, retching, pallor, lethargy, diaphoresis, and watery diarrhea (155). Michaud et al have reported the cases of 2 children with EA who presented with dumping syndrome without any known precipitating factors, such as fundoplication or associated microgastria (156). Previous reports of dumping syndrome in EA had so far been related to fundoplication (29). Studies have shown that abnormal gastric emptying is frequent in EA patients (74,157,158). Both abnormal gastric emptying and/or damage to the vagus nerve during esophageal anastomosis may lead to dumping syndrome (29,156).

• Transition to adulthood

The first generation of patients successfully operated for EA are reaching their sixth decade of life, highlighting that EA is becoming more and more an adult health issue. Moreover, since the late 1960s, >70% (and now >90%) of patients survive to adulthood. Therefore, a growing number of EA survivors are adults and focus on the long-term outcomes in these patients is necessary.

33. What are the long-term digestive morbidities of EA in adulthood?

Symptoms

In adult EA patients, ongoing GI symptoms are common, whereas respiratory problems are less frequent. Despite the frequency of these GI symptoms, it is striking that most adults born with EA have grown accustomed to living with a degree of dysphagia and reflux symptoms, and often do not consider them problematic enough to seek medical attention. This can result in suboptimal management of GER. Six case series reporting GI symptoms in adult patients older than 18 years have been so far reported (19,46,159–161). Only one compared 101 adult patients operated for EA with their native esophagus born between 1947 and 1985 (mean follow-up 36 years, range 22–57 years) with a random selected population of 287 control subjects (19).

a. Dysphagia: Symptoms of dysphagia are extremely frequent and affect 39% (31) to 85% (19) of adults; a significantly higher proportion than in control subjects (2%) (19). The roles of

dysmotility or residual stricture are not yet clear in adults. The benefit of dilation of strictures has not been established in this population.

b. Reflux: The prevalence of symptomatic GER is significantly higher among the patients than among controls (34% vs 8%), as reported by Sistonen (19). Taylor et al found that GER symptoms were reported by 63% of subjects, and 25% of these had severe reflux symptoms, defined as occurring at least 3 days/wk (159).

Statement 33a: Dysphagia and symptoms of GER continue into adulthood in EA patients, and are more frequent in EA survivors than in the general population.

Expert opinion
High level of evidence
VOTES: 9/9/9/9/9/9 Accepted

Esophagitis and Barrett Esophagus

Sistonen et al describe 101 patients with their native esophagus who systematically underwent upper GI endoscopy. GER symptoms and dysphagia were equally common in individuals with normal histology, histologic esophagitis, or epithelial metaplasia (19). Overall, endoscopic esophagitis was reported in 8% to 58%, histological esophagitis in 24% to 90% and macroscopic Barrett esophagus in 6% to 31%. Columnar epithelial metaplasia without goblet cells occurred in 0 to 19% of patients, and with goblet cells in 4% to 12%. Based on these findings, the prevalence of Barrett esophagus is at least 4-fold higher among the adult population with repaired EA compared with general population.

In a multivariate logistic regression analysis, Sistonen et al showed that surgically treated AS during infancy, LG requiring myotomy to enable primary anastomosis, recurrent TEF, AS in adulthood, and patient age were the most significant predictive factors for the occurrence of epithelial metaplasia with or without goblet cells. Surgical complications, patient age, and impaired esophageal motility were significant predictors of development of epithelial metaplasia (Table 3).

Statement 33b: The incidence of esophagitis and esophageal gastric and intestinal metaplasia (Barrett) is increased in adults with EA as compared with the general population.

Expert opinion
High level of evidence
VOTES: 9/9/9/9/9/9 Accepted

Cancer

To date, 8 case reports of esophageal cancer (3 adenocarcinoma (162–164), 5 squamous cell carcinoma (31,159,165,166)) occurring between 20 and 46 years have been reported. One cohort study in Finland revealed that the relative risk of esophageal cancer in adults operated for EA was lower than the calculated 500-fold higher risk when compared with the normal control population (167). A retrospective review of the EA database from the Royal Children's Hospital in Melbourne (798 patients [309 patients older than 40 years]) was performed to identify cases of esophageal cancer developing in this cohort. At the time of the publication, 4 of 309 patients had developed esophageal squamous cell carcinoma, for the age of 40 years. The cumulative incidence of esophageal squamous cell carcinoma in this age group was 50 times that expected in the general population (166). No adequately powered study has been published that measures the risk of developing cancer in adults with EA. Mitomycin, usually classified as an alkylating agent, used as an adjuvant therapy in the treatment of recurrent strictures in EA patients, may be an additional long-term risk factor and patients who have been treated with it warrant additional specific surveillance.

Statement 33c: While current studies show no increase incidence of esophageal cancer (adenocarcinoma, squamous cell carcinoma) in adults with EA, esophageal cancer remains a concern.

Expert opinion
Low level of evidence
VOTES: 9/9/9/9/9/9 Accepted

34. Is medical transitioning to adult medico-surgical services necessary?

Studies have shown that most adult patients with EA do not have any follow-up nor any contact with the hospital beyond childhood (31). Moreover, they do not seek medical attention for symptoms that have been present since infancy. Only 10% of patients are on appropriate treatment for GER; 34% are symptomatic but do not seek medical attention although they should be treated (19). Undertreatment leads to the high incidence of unrecognized esophagitis and gastric/intestinal metaplasia. Transitioning is essential to bridge from pediatric to adult care to ensure that comprehensive care is provided throughout the life of all patients with EA. It is essential to plan this transition with the adult health care physician who can be a general practitioner, a surgeon, a gastroenterologist, a pulmonologist, or any informed specialist aware of the specifics of the care of adults operated for EA. No study addresses transition issues in patients with EA.

Statement 34: We recommend transition of young adults from pediatric care to an adult physician with expertise in EA (general practitioner, surgeon, gastroenterologist, pulmonologist, or any informed specialist aware of the specificities of the care of adults operated for EA).

Expert opinion
No level of evidence
Votes: 8/8/8/9/9/9 Accepted

35. How should surveillance be managed in adult EA patients after transition from childhood? (Fig. 1, box 11)

The intended effect of surveillance is a comprehensive clinical and endoscopic screening system aiming to start treatment early when indicated, to prevent the development of esophageal malignancy, and to detect early signs of intestinal metaplasia and squamous cell carcinoma. Endoscopic surveillance should be performed: systematically every 5 to 10 years; if a new esophageal symptom occurs; and if regular symptoms (such as dysphagia) worsen. Early evidence of squamous cell carcinoma and adenocarcinoma of the esophagus are generally small, subtle mucosal abnormalities. Therefore, to optimize

TABLE 3. Studies conducted in adults >18 years with esophageal atresia

References	No. patients	Age, y	Dysphagia, %	Reflux symptoms, %	Patients who underwent endoscopy (N)	Endoscopic esophagitis, %	Histological esophagitis, %	Endoscopic Barrett esophagus, %	Gastric metaplasia, %	Intestinal metaplasia, %	Cancer (N)
Chetcuti et al (46)	125	18–39	53	46	NA	NA	NA	NA	NA	NA	NA
Krug et al (32)	39	18–26	77	33	34	26	24	6	0	6	0
Deurloo et al (31)	38	28–45	39	49	23	9	90	9	4	4	1 (squamous carcimoma)
Taylor et al (159)	132	20–48	52	63	62	58*	NA	26	15	11	1 (squamous carcimoma)
Sistonen et al (19)	101 (vs 287 controls)	22–57	85	34	101	8	25†	11	15	6	0
Hyunh-Trudeau et al (161)	41	18–44	73	29	32	19	25	31	19	12	0

NA = not available.
*Mild esophagitis, 8%; moderate esophagitis 40%; severe esophagitis 10%.
†Esophagitis mild in 22 patients, and moderate in 3 patients.

detection rates, advanced mucosal imaging techniques should be used. Acetic acid staining is a cheap and sensitive technique to accentuate the squamocolumnar junction. Chromoendoscopy with Lugol iodine sprayed onto the mucosal surface improves visualization of subtle squamous dysplasia from the surrounding normal mucosa because the iodine is not taken up by the dysplastic mucosa. Narrow band imaging has also been described detect early squamous cell carcinoma. In cases of endoscopic Barrett esophagus, 4 quadrants biopsies should be taken every centimeter.

No study reports the benefit of a systematic surveillance in adults with EA.

Statement 35: We recommend regular clinical follow-up in every adult patient with EA, with special reference to presence of dysphagia, GER, respiratory symptoms and anemia with:

1. **Routine endoscopy (with biopsies in 4 quadrants at gastroesophageal junction and anastomotic site) at time of transition into adulthood and every 5 to 10 years.**
2. **Additional endoscopy if new or worsening symptoms develop.**
3. **In presence of Barrett as per consensus recommendations.**

Expert opinion
No level of evidence
Votes: 9/9/8/8/7/9 Accepted

- **Quality of life**

36. Is quality of life (QOL) impaired in EA patients?

Children

Three noncontrolled studies have evaluated QoL in children and adolescents with EA. Peetsold et al reported global QoL scores to be similar to healthy controls. Children reported their general health perception as being affected by GER symptoms. Older age negatively affects health related-QoL (HRQoL) (20). Legrand et al, using a PedsQL score in 57 type C EA patients with a mean age of 13 years showed a lower score in EA patients when compared with healthy controls, but higher scores in comparison to patients with diabetes and other chronic diseases. Similarly, GER was an independent risk factor for poor QoL (18). Dingenman et al studied children and adults with complicated EA (delayed anastomosis, stricture requiring >10 dilations, major surgical revision, or esophageal replacement), and the childrens' families. Of note, these patients also had a high incidence (>90%) of associated malformations. The health related QoL was in the normal range in children with delayed anastomosis. The family impact was important, with 30% of parents scoring positive for suspected depression (168).

Adults

Ure et al reported 50 adults born between 1963 and 1971 (mean age 25y) with EA, without a control group. Those patients with primary anastomosis had unimpaired QOL (169). Deurloo et al reported 97 patients >16 years (range 16–48 years), with a response rate of 80%. No differences were noted in overall physical and mental health between EA patients and healthy subjects. EA patients, however, reported worse general health and less vitality than healthy subjects. 34% of patients perceived their QOL to be impaired due to GI symptoms (170).

Koivusalo et al studied patients born between 1947 and 1956 with isolated EA and few associated malformations (171). According to SF-36 and a visual analog scale, the health- related QoL of EA patients was not worse than that of general population. Only the GI quality of life index (GIQLI) dimension measuring GER was lower in EA patients.

Statement 36: Although GI and respiratory symptoms and associated comorbidities (esophageal replacement and congenital anomalies) may negatively impact HRQoL, no evidence currently shows that the overall HRQoL is impaired in children and adults with EA compared with the general population. We recommend long-term medical and psychosocial support for these patients and families.

Expert opinion
Moderate level of evidence
VOTES: 9/9/9/8/7/9 Accepted

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